STANFORD UNIVERSITY MEDICAL CENTER

国

STANFORD, CALIFORNIA 94305

STANFORD UNIVERSITY SCHOOL OF MEDICINE Department of Genetics (413) 497-3052

August 6, 1974

Professor G.F. Gause Institute of New Antibiotics Academy of Medical Sciences Bolshaya Pirogovskay 11 Moscow

Dear Professor Gause,

I am sorry to have missed a chance to see you again if, as I could not, you attended the last sessions of ACMR/WHO in June. (Martin Kaplan may have told you the reason - a new daughter who is a great joy to my wife and myself)

In particular, I wished to discuss with you your current views on macromutants. Do you continue to get reproducible results with paracoli 5099, of do you get sporadic effects that make it hard to settle whether contamination is or is not the basis? I have not found papers from you later than 1971 that would help bring me up to date on your current views.

One thought that has occurred to me, but might be quickly discounted, is that the "macromutant" is a parasitic Bdellovibrio-like species, capable of occasional mutation to a host-independent form (cf. R.J. Seidler and M.P. Starr, J.Bact. 100:769-785, 1969).

I very much appreciated the cautions (in your 1968 review in <u>Prog. Nucl. Acids</u>) about dogmatism. Your example about lysogeny was an apt one, as you may know from my own work on this subject (cf. <u>Ann. Rev. Microbiol. 4:1-22, 1949; Genetics</u> 38:51, 1953). The validity of observations on macromutants certainly deserves to be settled on an empirical basis, not by allusions to miracles.

If your own data have not led to more definite conclusions since 1971, I would be happy to offer certain additional suggestions about alternative approaches, but they depend on the reproducibility of occurrence of the macromutants in your own laboratory.

Yours sincerely

Joshua Lederberg

Professor of Genetics

JL/rk